

Amendment and Response

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- nucleotide sequence, the complement of which hybridizes to the nucleotide sequence set forth at SEQ ID NO:1 in a hybridization solution at 60°C for 3 hours, followed by two washes for 15 minutes each at room temperature in a solution containing 2x SSC and 0.05 % SDS, followed by two washes for 15 minutes each at 50°C in a solution containing 0.1% SSC and 0.1% SDS;
- (b) extending the primers to form complementary primer extension products which act as templates for synthesizing the desired DNA fragment containing the repeat region;
 - (c) detecting the fragment so amplified; and
 - (d) analyzing the amplified DNA fragment for an at-risk allele having at least about 80 CTG repeats in the repeat region or at least about 92 combined CTA and CTG repeats in the repeat region.

2. (Amended) A method for detecting the presence of a DNA fragment located within an at-risk allele of the SCA8 coding sequence comprising:

- (a) treating separate complementary DNA molecules of a DNA fragment containing a repeat region of the SCA8 coding sequence with a molar excess of two oligonucleotide primers wherein a first oligonucleotide primer of the two oligonucleotide primers is chosen from nucleotides 1-448 of SEQ ID NO:1, and a second oligonucleotide primer of the two oligonucleotide primers is chosen from nucleotides complementary to nucleotides 726-1,159 of SEQ ID NO:1, wherein each primer has at least 11 nucleotides;
- (b) extending the primers to form complementary primer extension products which act as templates for synthesizing the desired DNA fragment containing the repeat region;
- (c) detecting the fragment so amplified; and
- (d) analyzing the amplified DNA fragment for an at-risk allele having at least about 80 CTG repeats in the repeat region or at least about 92 combined CTA and CTG

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repeats in the repeat region.

3. (Amended) A method for detecting the presence of a DNA fragment located within an at-risk allele of the SCA8 coding sequence comprising:
- (a) treating separate complementary DNA molecules of a DNA fragment containing a repeat region of the SCA8 coding sequence with a molar excess of two oligonucleotide primers wherein the first oligonucleotide primer is selected from the group consisting of SEQ ID NO:5, SEQ ID NO:8, and SEQ ID NO:4 and wherein the second oligonucleotide primer is selected from the group consisting of SEQ ID NO:6, SEQ ID NO:9, and SEQ ID NO:12;
 - (b) extending the primers to form complementary primer extension products which act as templates for synthesizing the desired DNA fragment containing the repeat region;
 - (c) detecting the fragment so amplified; and
 - (d) analyzing the amplified DNA fragment for an at-risk allele having at least about 80 CTG repeats in the repeat region or at least about 92 combined CTA and CTG repeats in the repeat region.

7. (Amended) A method for detecting the presence of at least one DNA molecule containing a repeat region of an SCA8 coding sequence comprising:
- (a) digesting genomic DNA with a restriction endonuclease to obtain DNA fragments;
 - (b) denaturing the DNA fragments to yield DNA molecules and probing the DNA molecules under hybridizing conditions with a detectably labeled probe, which hybridizes to a DNA molecule containing a repeat region of an isolated SCA8 coding sequence, wherein the SCA8 coding sequence comprises a nucleotide sequence, the complement of which hybridizes to the nucleotide sequence set forth at SEQ ID NO:1 in a hybridization solution at 60°C for 3 hours, followed by

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two washes for 15 minutes each at room temperature in a solution containing 2x SSC and 0.05 % SDS, followed by two washes for 15 minutes each at 50°C in a solution containing 0.1% SSC and 0.1% SDS;

- (c) detecting the probe which has hybridized to the DNA molecule; and
- (d) analyzing the DNA molecule for a repeat region characteristic of a normal or at-risk form of the SCA8 coding sequence.

13. (Twice Amended) A method for determining whether an individual is not at-risk for developing spinocerebellar ataxia type 8, the method comprising analyzing a repeat region of a spinocerebellar ataxia type 8 coding sequence wherein individuals who are not at-risk for developing spinocerebellar ataxia type 8 have less than 80 CTG repeats in the repeat region or no greater than about 91 combined CTA and CTG repeats in the repeat region, wherein the SCA8 coding sequence comprises a nucleotide sequence, the complement of which hybridizes to the nucleotide sequence set forth at SEQ ID NO:1 in a hybridization solution at 60°C for 3 hours, followed by two washes for 15 minutes each at room temperature in a solution containing 2x SSC and 0.05 % SDS, followed by two washes for 15 minutes each at 50°C in a solution containing 0.1% SSC and 0.1% SDS.

14. (Twice Amended) A method for detecting the presence of a DNA fragment located within an at-risk allele of the SCA8 coding sequence comprising:
- (a) treating separate complementary DNA molecules of a DNA fragment containing a repeat region of the SCA8 coding sequence with a molar excess of a first oligonucleotide primer pair, wherein the SCA8 coding sequence comprises a nucleotide sequence, the complement of which hybridizes to the nucleotide sequence set forth at SEQ ID NO:1 in a hybridization solution at 60°C for 3 hours, followed by two washes for 15 minutes each at room temperature in a solution containing 2x SSC and 0.05 % SDS, followed by two washes for 15 minutes each at 50°C in a solution containing 0.1% SSC and 0.1% SDS;

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- ~~(b) extending the first primer pair to form complementary primer extension products which act as templates for synthesizing a first desired DNA fragment containing the repeat region;~~
 - ~~(c) removing the first desired DNA fragment containing the repeat region;~~
 - ~~(d) treating separate complementary strands of the first desired DNA fragment containing the repeat region with a molar excess of a second oligonucleotide primer pair;~~
 - ~~(e) extending the second primer pair to form complementary primer extension products which act as templates for synthesizing a second desired DNA fragment containing the repeat region;~~
 - ~~(f) detecting the second desired DNA fragment so amplified; and~~
 - ~~(g) analyzing the amplified DNA fragment for an at-risk allele having at least about 80 CTG repeats in the repeat region or at least about 92 combined CTA and CTG repeats in the repeat region.~~

15. (Amended) A method for detecting the presence of a DNA fragment located within an at-risk allele of the SCA8 coding sequence comprising:

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- ~~(a) treating separate complementary DNA molecules of a DNA fragment containing a repeat region of the SCA8 coding sequence with a molar excess of a first oligonucleotide primer pair wherein the first oligonucleotide primer pair comprises a first oligonucleotide primer chosen from nucleotides 1-448 of SEQ ID NO:1, and a second oligonucleotide primer chosen from nucleotides complementary to nucleotides 726-1,159 of SEQ ID NO:1, wherein each primer has at least 11 nucleotides;~~
 - ~~(b) extending the first primer pair to form complementary primer extension products which act as templates for synthesizing a first desired DNA fragment containing the repeat region;~~
 - ~~(c) removing the first desired DNA fragment containing the repeat region;~~
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- (d) treating separate complementary strands of the first desired DNA fragment containing the repeat region with a molar excess of a second oligonucleotide primer pair;
- (e) extending the second primer pair to form complementary primer extension products which act as templates for synthesizing a second desired DNA fragment containing the repeat region;
- (f) detecting the second desired DNA fragment so amplified; and
- (g) analyzing the amplified DNA fragment for an at-risk allele having at least about 80 CTG repeats in the repeat region or at least about 92 combined CTA and CTG repeats in the repeat region.

17. (Amended) A method for detecting the presence of a DNA fragment located within an at-risk allele of the SCA8 coding sequence comprising:
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- (a) treating separate complementary DNA molecules of a DNA fragment containing a repeat region of the SCA8 coding sequence with a molar excess of a first oligonucleotide primer pair;
- (b) extending the first primer pair to form complementary primer extension products which act as templates for synthesizing a first desired DNA fragment containing the repeat region;
- (c) removing the first desired DNA fragment containing the repeat region;
- (d) treating separate complementary strands of the first desired DNA fragment containing the repeat region with a molar excess of a second oligonucleotide primer pair wherein the second oligonucleotide primer pair comprises a first oligonucleotide primer chosen from nucleotides 449-725 of SEQ ID NO:1, and a second oligonucleotide primer chosen from nucleotides complementary to nucleotides 726-1,159 of SEQ ID NO:1, wherein each primer has at least 11 nucleotides;
- (e) extending the second primer pair to form complementary primer extension
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- products which act as templates for synthesizing a second desired DNA fragment containing the repeat region;
- (f) detecting the second desired DNA fragment so amplified; and
 - (g) analyzing the amplified DNA fragment for an at-risk allele having at least about 80 CTG repeats in the repeat region or at least about 92 combined CTA and CTG repeats in the repeat region.

10.11 (Amended) A method for detecting the presence of a DNA fragment located within an at-risk allele of the SCA8 coding sequence comprising:

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- (a) treating separate complementary DNA molecules of a DNA fragment containing a repeat region of the SCA8 coding sequence with a molar excess of a first oligonucleotide primer pair;
 - (b) extending the first primer pair to form complementary primer extension products which act as templates for synthesizing a first desired DNA fragment containing the repeat region;
 - (c) removing the first desired DNA fragment containing the repeat region;
 - (d) treating separate complementary strands of the first desired DNA fragment containing the repeat region with a molar excess of a second oligonucleotide primer pair wherein the second oligonucleotide primer pair comprises a first oligonucleotide primer that has three CTA repeats followed by three CTG repeats and a second oligonucleotide primer chosen from nucleotides complementary to nucleotides 726-1,159 of SEQ ID NO:1;
 - (e) extending the second primer pair to form complementary primer extension products which act as templates for synthesizing a second desired DNA fragment containing the repeat region;
 - (f) detecting the second desired DNA fragment so amplified; and
 - (g) analyzing the amplified DNA fragment for an at-risk allele having at least about 80 CTG repeats in the repeat region or at least about 92 combined CTA and CTG
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repeats in the repeat region.

21. (Twice Amended) An isolated SCA8 coding sequence comprising a repeat region wherein the SCA8 locus is located on the long arm of chromosome 13, and a complement of the coding sequence, wherein the SCA8 coding sequence comprises a nucleotide sequence, the complement of which hybridizes to the nucleotide sequence set forth at SEQ ID NO:1 in a hybridization solution at 60°C for 3 hours, followed by two washes for 15 minutes each at room temperature in a solution containing 2x SSC and 0.05 % SDS, followed by two washes for 15 minutes each at 50°C in a solution containing 0.1% SSC and 0.1% SDS.

23. (Amended) An isolated oligonucleotide consisting essentially of at least 15 nucleotides from nucleotides 1-448 of SEQ ID NO:1, and the complementary nucleotides thereto.

24. (Amended) An isolated oligonucleotide consisting essentially of at least 15 nucleotides from nucleotides 726-1,159 of SEQ ID NO:1, and the complementary nucleotides thereto.

25. (Three Times Amended) An isolated oligonucleotide that specifically hybridizes to a nucleic acid molecule comprising a repeat region of an isolated SCA8 coding sequence; the oligonucleotide having at least about 11 nucleotides, wherein the SCA8 coding sequence comprises a nucleotide sequence, the complement of which hybridizes to the nucleotide sequence set forth at SEQ ID NO:1 in a hybridization solution at 60°C for 3 hours, followed by two washes for 15 minutes each at room temperature in a solution containing 2x SSC and 0.05 % SDS, followed by two washes for 15 minutes each at 50°C in a solution containing 0.1% SSC and 0.1% SDS.

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38. (Amended) A method for detecting the presence of a DNA fragment located within a not at-risk allele of the SCA8 coding sequence comprising:

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- (a) treating separate complementary DNA molecules of a DNA fragment containing a repeat region of the SCA8 coding sequence with a molar excess of two oligonucleotide primers, wherein the SCA8 coding sequence comprises a nucleotide sequence, the complement of which hybridizes to the nucleotide sequence set forth at SEQ ID NO:1 in a hybridization solution at 60°C for 3 hours, followed by two washes for 15 minutes each at room temperature in a solution containing 2x SSC and 0.05 % SDS, followed by two washes for 15 minutes each at 50°C in a solution containing 0.1% SSC and 0.1% SDS;
 - (b) extending the primers to form complementary primer extension products which act as templates for synthesizing the desired DNA fragment containing the repeat region;
 - (c) detecting the fragment so amplified; and
 - (d) analyzing the amplified DNA fragment for a not at-risk allele having less than 80 CTG repeats in the repeat region or no greater than about 91 combined CTA and CTG repeats in the repeat region.

39. (Amended) A method for detecting the presence of a DNA fragment located within a not at-risk allele of the SCA8 coding sequence comprising:

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- (a) treating separate complementary DNA molecules of a DNA fragment containing a repeat region of the SCA8 coding sequence with a molar excess of a first oligonucleotide primer pair, wherein the SCA8 coding sequence comprises a nucleotide sequence, the complement of which hybridizes to the nucleotide sequence set forth at SEQ ID NO:1 in a hybridization solution at 60°C for 3 hours, followed by two washes for 15 minutes each at room temperature in a solution containing 2x SSC and 0.05 % SDS, followed by two washes for 15 minutes each at 50°C in a solution containing 0.1% SSC and 0.1% SDS;

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- is not*
- (b) extending the first primer pair to form complementary primer extension products which act as templates for synthesizing a first desired DNA fragment containing the repeat region;
 - (c) removing the first desired DNA fragment containing the repeat region;
 - (d) treating separate complementary strands of the first desired DNA fragment containing the repeat region with a molar excess of a second oligonucleotide primer pair;
 - (e) extending the second primer pair to form complementary primer extension products which act as templates for synthesizing a second desired DNA fragment containing the repeat region;
 - (f) detecting the second desired DNA fragment so amplified; and
 - (g) analyzing the amplified DNA fragment for a not at-risk allele having less than 80 CTG repeats in the repeat region or no greater than about 91 combined CTA and CTG repeats in the repeat region.

40.15 (Amended) A method for determining whether an individual is at-risk for developing spinocerebellar ataxia type 8, the method comprising analyzing a repeat region of a spinocerebellar ataxia type 8 coding sequence wherein individuals who are at-risk for developing spinocerebellar ataxia type 8 have at least about 80 CTG repeats in the repeat region or at least about 92 combined CTA and CTG repeats in the repeat region.

49.37 (Amended) The method of claim *13^e* wherein the analyzing comprises sequencing the repeat region of a spinocerebellar ataxia type 8 coding sequence, wherein the spinocerebellar ataxia type 8 coding sequence comprises a nucleotide sequence, the complement of which hybridizes to the nucleotide sequence set forth at SEQ ID NO:1 in a hybridization solution at 60°C for 3 hours, followed by two washes for 15 minutes each at room temperature in a solution containing 2x SSC and 0.05 % SDS, followed by two washes for 15 minutes each at 50°C in a solution containing 0.1% SSC and 0.1% SDS.

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§2. 23 (New) A method for determining whether an individual has spinocerebellar ataxia type 8, the method comprising analyzing a repeat region of a spinocerebellar ataxia type 8 coding sequence wherein individuals who are at-risk for developing spinocerebellar ataxia type 8 have at least about 80 CTG repeats in the repeat region or at least about 92 combined CTA and CTG repeats in the repeat region, and wherein the individual displays at least one symptom of ataxia.

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